In silico identification of potential inhibitors for human aurora kinase b

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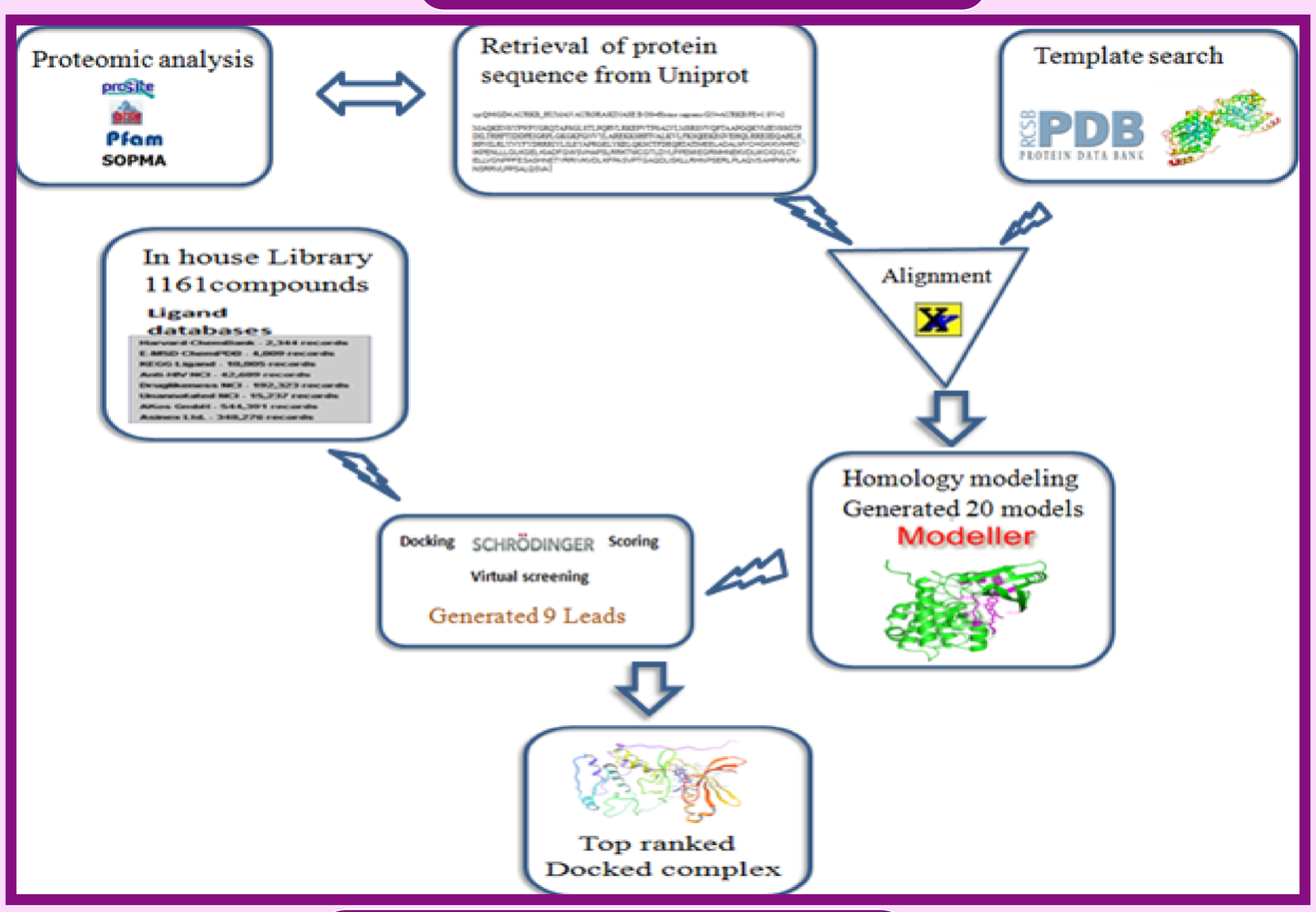
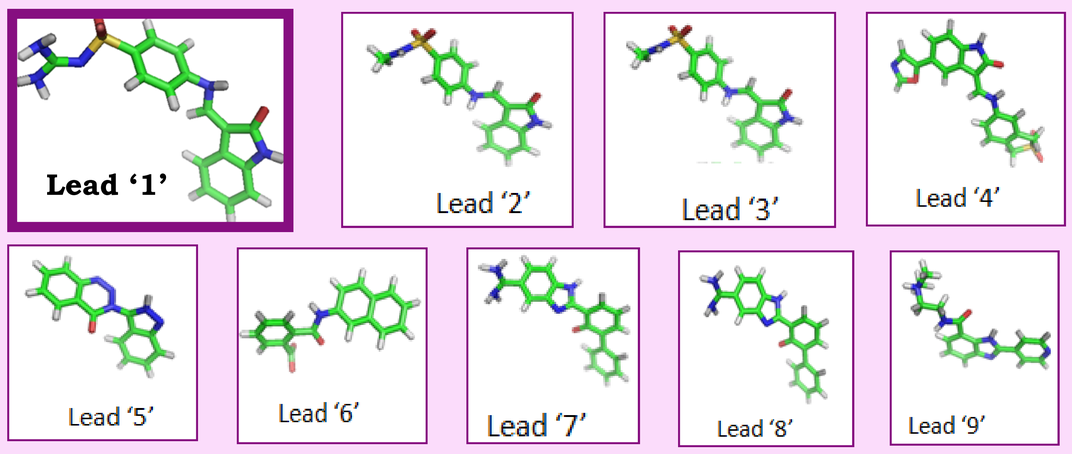
Key points

- Cell cycle progression through mitosis and meiosis involves regulation by serine or threonine kinases from aurora family.
- Human aurora kinase b (AURKB) is a protein mainly involved in the proper segregation of chromosomes during mitosis as well as meiosis.
- Over expression of AURKB leads to the unequal distribution of genetic information creating a aneuploid cells, a hallmark of cancer. and this heads to genetic instability is linked on primary non-small cell lung carcinoma.
- Inhibition of AURKB results inhibition of cytokinesis (or anticytokinesis), hence is an attractive anticancer strategy.
- *In silico* work was carried out to identify novel potent inhibitors towards human AURKB.

Material and methods





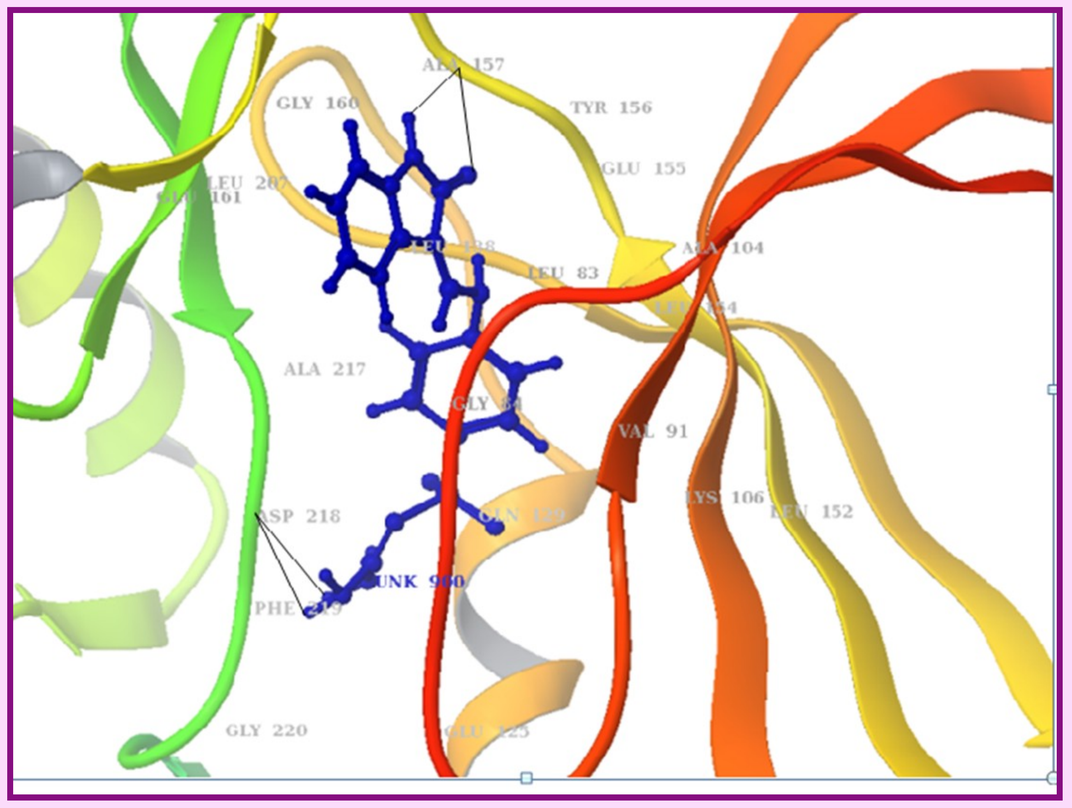
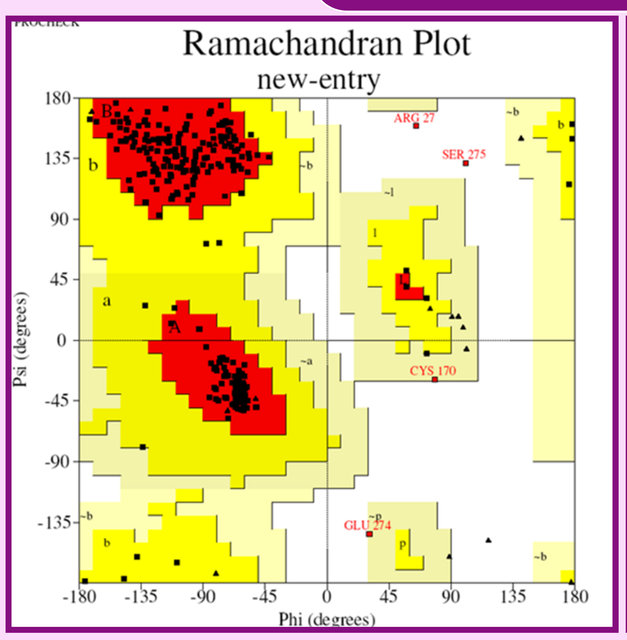
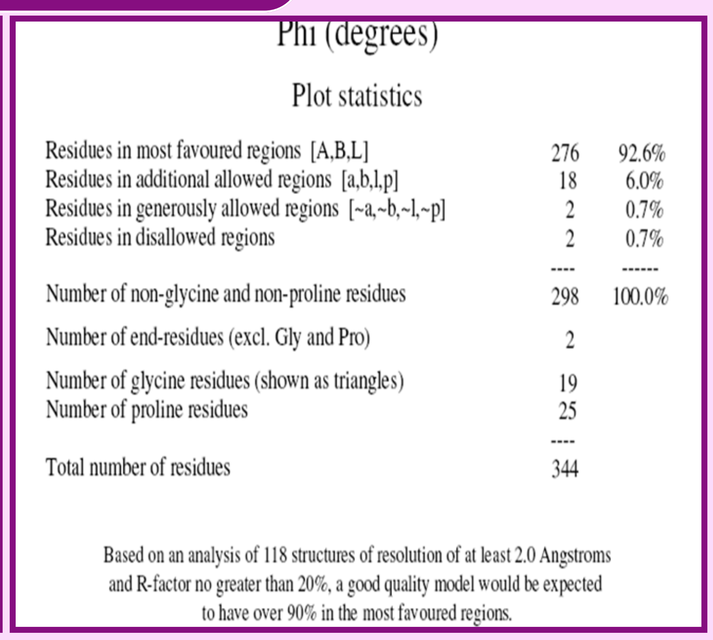


Figure 4: Nine lead molecules and Lead1- AURKB docking complex. The docking complex revealed that two amino acid residues ASP 218 (two Hydrogen bonds) and ALA 157 of active sites were directly involved in formation of hydrogen bond network. The active site residues detected from crystal structure also interacted with lead1 through good van der Waal contacts.

Results and Discussion





Phi (degrees)

Plot statistics

Residues in most favoured regions [A,B,L]	276	92.6%
Residues in additional allowed regions [a,b,l,p]	18	6.0%
Residues in generously allowed regions [~a,~b,~l,~p]	2	0.7%
Residues in disallowed regions	2	0.7%
Number of non-glycine and non-proline residues	298	100.0%
Number of end-residues (excl. Gly and Pro)	2	
Number of glycine residues (shown as triangles)	19	
Number of proline residues	25	
Total number of residues	344	

Based on an analysis of 118 structures of resolution of at least 2.0 Angstroms and R-factor no greater than 20%, a good quality model would be expected to have over 90% in the most favoured regions.

Figure 1: Ramachandran plot for modeled Human AURKB

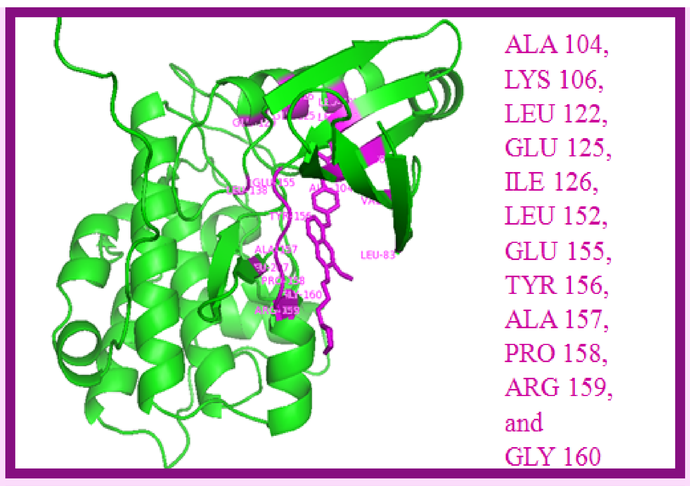


Figure 2: Modeled structure of AURKB with PDB ligand 2 deciphering active site residues visualized through PyMol

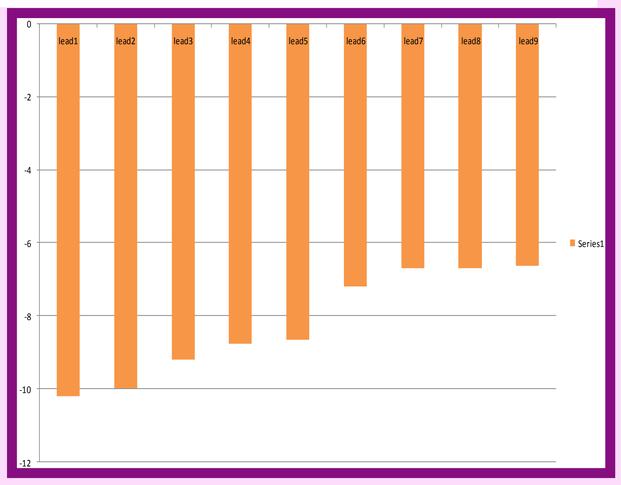


Figure 3: Graphical representation of XP Gscores.

Conclusion

- Analysis of the Aurkb 3D model had revealed that ALA 157 an essential amino acid for AURKB activity is directly getting blocked by lead 1 by forming hydrogen bond and good van der wall interactions.
- Thus it would be highly effective as a novel inhibitor towards of human AURKB protein for treatment of metastasis.

Acknowledgement

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